From: Calvin Willhite
To: NICEATMNews
Subject: Re: Input Requested on U.S. Strategic Roadmap for New Approaches to Evaluating Chemical Safety
Date: Friday, March 31, 2017 5:31:00 PM

Dear Sir or Madam,

I am writing to NTP in response to the request shown below. I am writing to make a practical suggestion that is intended to direct NICEATM and ICCVAM to demonstrate universal acceptance of certain in vitro data in human health risk assessment. Human health risk assessments are as you know used to develop public health 'guidelines', Agency reference concentrations and in some instances enforceable limits (e.g., drinking water maximum contaminant levels; MCLs).

In 2012 the State of Pennsylvania made inquiry of me regarding Acute Exposure Guideline Levels for a series of ~ 10 substances that are intentionally added to drinking water as part of routine municipal water disinfection and treatment. The State asked these levels be considered acute "do not use" and "do not consume" concentrations that the State could use in case of accidental or intentional [e.g., terrorist] adulteration of community drinking water to issue warnings to consumers of the water.

The results of 3 such assessments were published in 2013 (Human and Experimental Toxicology 32(3): 241-259, 260-274 and 275-298). There are dozens of such substances including materials like sodium hypochlorite (common bleach). The "do not use" values are based on skin and eye irritation and most often are derived from very old (often incomplete) rabbit skin and eye corrosion data.

My suggestion is that NICEATM and ICCVAM compile all available controlled rabbit (and other species as
available) eye and skin toxicity data and complete comparisons to the in vitro (e.g., bovine eye) data with the goal of "validating" the in vitro rabbit results to in vitro data. The in vitro data for direct contact irritants/corrosion are very valuable and make the most direct (and non-controversial) extrapolation to use in human health risk assessment. No doubt the correlation between in vitro and in vivo data for skin and eye irritants will be very strong indeed. It is possible that one in vitro protocol might be more useful or efficient than another or that a weight of evidence method may be needed where we are fortunate to have multiple in vitro results for particular class of materials.

Should regulatory agencies like US EPA adopt the in vitro data packages for regulatory application, this will make a positive demonstration of all the financial resources and efforts carried out by NICEATM and ICCVAM over the past many years. Once we have a firm demonstration of broad application of the in vitro data for direct contact exposure circumstances, we can move on to more complicated ingestion routes of exposure. My point here is that demonstration of real, practical utility of the NICEATM/ICCVAM efforts is needed prior to tackling substances and routes of exposure where difficult aspects of absorption, metabolism, distribution and different target organs and responses complicate the tasks at hand.

Thank you,

Calvin Willhite, PhD

From: NTP Interagency Center for the Evaluation of Alternative Toxicological Methods <NICEATM-L@LIST.NIH.GOV> on behalf of NICEATM News <niceatmnews@MAIL.NIH.GOV>
Sent: Friday, March 31, 2017 11:51 AM
To: NICEATM-L@LIST.NIH.GOV
Subject: Input Requested on U.S. Strategic Roadmap for New Approaches to Evaluating Chemical Safety

NICEATM News - March 31, 2017

Input Requested on U.S. Strategic Roadmap for New Approaches to Evaluating Chemical Safety

ICCVAM is coordinating the development of a strategic roadmap for incorporating new approaches into safety testing of chemicals and medical products in the United States. This effort will increase confidence in alternative methods and improve their relevance to human health outcomes. The effort will also maximize efficiency while maintaining a commitment to replace, reduce, and refine animal use. Federal agencies, the regulated community, non-governmental organizations, and other technical experts will work together to (1) help guide the development of new tools, based on new science and technology, to support regulatory and research needs; (2) use knowledge of human and animal biology as appropriate for establishing confidence in new approaches; and (3) help facilitate and encourage the implementation and use of these new approaches by federal agencies and regulated industries.

On behalf of ICCVAM, NICEATM invites interested persons to provide input relevant to this effort. Submit comments by email to ICCVAMquestions@niehs.nih.gov by August 31. Comments should include the commenter's name, affiliation (if applicable), mailing address, telephone, email, and sponsoring organization (if any). Guidelines for submitting public comments and more information about the strategic roadmap are available on the NICEATM website at https://ntp.niehs.nih.gov/go/natl-strategy. Comments submitted will be posted on this page.

The ICCVAM Public Forum on May 23 will provide an opportunity for comment on this effort and other ICCVAM agency activities. The public forum will be held at the National Institutes of Health in Bethesda, MD, and webcast. More information about the public forum is available at https://ntp.niehs.nih.gov/go/iccvamforum-2017. Two meetings later in 2017 will also offer opportunities for public comment on the strategic roadmap: the NTP Board of Scientific Counselors meeting on June 29 at NIEHS, and the annual meeting of the Scientific Advisory Committee on Alternative Toxicological Methods on September 18 and 19 in the Washington, DC area.

The NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) supports the development and evaluation of new, revised, and alternative methods to identify potential hazards to human health and the environment, with a focus on replacing, reducing, or refining animal use. NICEATM provides support to the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM).